Application No. 10/633,407 Response dated

AMENDMENTS TO THE CLAIMS

Docket No.: 58098(71417)

1. (Currently amended) A method for modulating endothelial cell (EC) proliferation in a mammal, wherein the method comprises decreasing ezrin activity in the mammal by an amount sufficient to promote proliferation of the cells by administering to the mammal an ezrin modulating agent before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, wherein the method comprises isolating endothelial progenitor cells (EPCs) from the mammal and contacting the EPCs with at least one of: an ezrin modulating agent, cytokine, angiogenic factor or hematopoetic factor.

2-16. (Cancelled)

Office Action of May 26, 2009

17. (Currently amended) A method for inducing formation of new blood vessels in a mammal, the method comprising decreasing ezrin activity in an amount sufficient to induce formation of the new blood vessels in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in mammalian cells before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, wherein the method comprises isolating endothelial progenitor cells (EPCs) from the mammal and contacting the EPCs with at least one of: an ezrin modulating agent, cytokine, angiogenic factor or hematopoetic factor.

18-23. (Cancelled)

- 24. (Currently amended) A method for inducing formation of new blood vessels in a mammal, the method comprising decreasing ezrin activity in an amount sufficient to induce formation of the new blood vessels in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in mammalian cells before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels. The method of claim 17, wherein the mammal has, is suspected of having, or will have ischemic tissue.
- 25. (Original) The method of claim 24, wherein the tissue is associated with an ischemic vascular disease.

Application No. 10/633,407 Docket No.: 58098(71417)
Response dated

Office Action of May 26, 2009

26. (Currently amended) A method for modulating endothelial cell (EC) proliferation in a mammal, wherein the method comprises decreasing ezrin activity in the mammal by an amount sufficient to promote proliferation of the cells by administering to the mammal an ezrin modulating agent before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, The method of claim 1 or 17, wherein the method further comprises administering to the mammal at least one of an angiogenic protein, cytokine, hematopoietic protein, or an effective fragment thereof.

27. (Previously presented) The method of claim 26, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TFG- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoetin-1 (Ang1) or nitric oxide synthase (NOS).

28-29. (Cancelled)

30. (Currently amended) A method for reducing the severity of blood vessel damage in a mammal, wherein the method comprises decreasing ezrin activity in endothelial cells (EC) before, during or after the mammal is exposed to conditions conducive to damaging the blood vessels, wherein the decrease in ezrin activity is sufficient to reduce the severity of the blood vessel damage in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in endothelial cells, wherein the method comprises isolating endothelial progenitor cells (EPCs) from the mammal and contacting the EPCs with at least one of: an ezrin modulating agent, cytokine, angiogenic factor or hematopoetic factor.

31-37. (Cancelled)

38. (Currently amended) <u>A method for reducing the severity of blood vessel damage in a mammal</u>, wherein the method comprises decreasing ezrin activity in endothelial cells (EC) before,

Application No. 10/633,407 Response dated

Office Action of May 26, 2009

during or after the mammal is exposed to conditions conducive to damaging the blood vessels, wherein the decrease in ezrin activity is sufficient to reduce the severity of the blood vessel damage in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in endothelial cells, wherein the method further comprises administering to the mammal at least one ezrin modulating agent sufficient to decrease ezrin DNA binding activity relative to a control, wherein the blood vessel damage is restenosis associated with an invasive manipulation, wherein the invasive manipulation is balloon angioplasty, or deployment of stent or catheter, The method of claim 37, wherein the stent is an endovascular stent.

Docket No.: 58098(71417)

39. (Currently amended) A method for reducing the severity of blood vessel damage in a mammal, wherein the method comprises decreasing ezrin activity in endothelial cells (EC) before, during or after the mammal is exposed to conditions conducive to damaging the blood vessels, wherein the decrease in ezrin activity is sufficient to reduce the severity of the blood vessel damage in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in endothelial cells, wherein the method comprises administering to the mammal at least one ezrin modulating agent sufficient to decrease ezrin DNA binding activity relative to a control, wherein the blood vessel damage is restenosis associated with ischemia, The method of claim 36, wherein the ischemia is associated with at least one of infection, trauma, graft rejection, cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy, or myocardial ischemia.

40-66. (Cancelled)

- 67. (Currently amended) The method of claim [[66]]1, 17, or 30, wherein the method further comprises administering the EPCs to the mammal in an amount sufficient to modulate endothelial cell proliferation.
- 68. (Original) The method of claim 67, wherein the method further comprises administering at least one of the following to the mammal before, during of after administration of the EPCs: ezrin modulating agent, cytokine, angiogenic factor or hematopoetic factor.

Application No. 10/633,407 Docket No.: 58098(71417)

Response dated Office Action of May 26, 2009

69-80. (Cancelled)

81. (Currently amended) A method for modulating endothelial cell (EC) proliferation in a mammal, wherein the method comprises decreasing ezrin activity in the mammal by an amount sufficient to promote proliferation of the cells by administering to the mammal an ezrin modulating agent before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, The method of claim 1, wherein ezrin activity is increased or decreased by contacting endothelial cells *ex vivo* with an ezrin modulating agent.

- 82. (Currently amended) A method for inducing formation of new blood vessels in a mammal, the method comprising decreasing ezrin activity in an amount sufficient to induce formation of the new blood vessels in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in mammalian cells before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, wherein the method further comprises administering to the mammal at least one ezrin modulating agent sufficient to decrease ezrin DNA binding activity relative to a control, wherein the method comprises contacting endothelial cells (ECs) with the ezrin modulating agent thereby decreasing ezrin activity in the cells, The method of claim 21, wherein the endothelial cells are contacted *ex vivo* with an-the ezrin modulating agent.
- 83. (Currently amended) A method for reducing the severity of blood vessel damage in a mammal, wherein the method comprises decreasing ezrin activity in endothelial cells (EC) before, during or after the mammal is exposed to conditions conducive to damaging the blood vessels, wherein the decrease in ezrin activity is sufficient to reduce the severity of the blood vessel damage in the mammal by administering to the mammal an ezrin modulating agent that decreases ezrin activity in endothelial cells, The method of claim 30, wherein ezrin activity is decreased by contacting endothelial cells *ex vivo* with an the ezrin modulating agent.
- 84. (New) A method for inducing formation of new blood vessels in a mammal, the method comprising decreasing ezrin activity in an amount sufficient to induce formation of the new blood vessels in the mammal by administering to the mammal an ezrin modulating agent that

Application No. 10/633,407 Docket No.: 58098(71417)

Response dated

Office Action of May 26, 2009

decreases ezrin activity in mammalian cells before, during, or after the mammal is exposed to conditions conducive to damaging blood vessels, wherein the method comprises administering to the mammal at least one of an angiogenic protein, cytokine, hematopoietic protein, or an effective fragment thereof.

85. (New) The method of claim 84, wherein the angiogenic protein is acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TFG- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), angiopoetin-1 (Ang1) or nitric oxide synthase (NOS).